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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/584,445	06/22/2006	Elie Leverd	3493-0170PUS1	4148

2292 7590 01/26/2009

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EXAMINER	
THOMAS, TIMOTHY P	
ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
01/26/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/584,445	LEVERD ET AL.	
	Examiner	Art Unit	
	TIMOTHY P. THOMAS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 12-16* is/are pending in the application.

4a) Of the above claim(s) *10,12 and 16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 13-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

1. Applicants' arguments, filed 10/23/2008, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

2. Applicant's arguments with respect to the drawings have been fully considered but they are not persuasive:

The drawings are objected to under 37 CFR 1.83(a) because the amended Figure 1 still fails to show all 7 sets of data named in the key and described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as “amended.” If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the

remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either “Replacement Sheet” or “New Sheet” pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

3. Applicant's arguments with respect to the unity of invention have been fully considered but they are not persuasive.

Applicant continues to argue the reasons indicated in the response files 1/28/2008 apply. These have been addressed and the requirement made final in the prior Office Action. The request for rejoinder is not made at this time, because the elected species are not currently allowable.

4. Applicant's arguments with respect to the rejection of claims 1-3, 7, 9 and 13 under 25 USC 103 have been fully considered but they are not persuasive:

Claims 1-3, 7, 9 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over GlaxoSmithKline (“Prescribing Information: Navelbine (vinorelbine tartrate) Injection: 2002 Nov; pp. 1-17; IDS 1/22/2008 reference CA) and Duflos et al. (US 6,127,377; 2000; IDS 10/4/2006 reference AB).

The rejection is maintained for the reasons of record.

Applicant argues that the substitution of vinorelbine ditartrate with vinflunine ditartrate would not have been predictable in view of the significant differences in physical and chemical properties between the two compounds; a list of differences is described, which includes: solubility, different degradation properties of the powder

forms, different major impurity products, different manufacturing processes, differences in antifungal activity. It is noted that no evidence is provided supporting such differences; therefore, arguments based on these characteristics are unpersuasive. Applicant further argues that even if the references are combined there fails to be any recognition of advantageously improved storage stability properties evidenced by Examples 1 and 2 of the present specification. It is noted that Example 1 compares a solid form to a solution form, a comparison not relevant for demonstrating unexpected results over the prior art combination rendering a solution obvious. Example 2 compares solutions containing citrate buffer at various pH values to unbuffered aqueous solution. Since the prior art combination renders an aqueous solution obvious (without buffer and without any preservatives or additives), this comparison does not provide evidence of unexpected results over the suggestion of the prior art; additionally Navelbine is taught to be stable until the product expiration date when stored at refrigerator temperatures and protected from light. Considering the similarity of the two molecules as vinca alkaloids, this would certainly imply similar stability for the related vinflunine ditatrate solution.

5. Applicant's arguments with respect to the rejection of Claims 1-2, 4-7, 9 and 13 under 35 USC 103 have been fully considered but they are not persuasive:

Claims 1-2, 4-7, 9 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wolgemuth (CA-2,001,643; 1990; IDS 10/4/2006 reference BC) and Duflos et al. (US 6,127,377; 2000; IDS 10/4/2006 reference AB).

The rejection is maintained for the reason of record and the following, addressed necessitated by the claim amendment: with respect to the amended exclusion of any sugar or sugar-based polyol, Wolgemuth teaches solutions may contain minor amounts of excipients such as sugar or polyols deriveved from sugars ("may contain" language implies embodiments where such sugars and polyols are absent; p. 4, lines 30-34). The fact that the preservative is not required (abstract) implies that the presence of a sugar makes no difference on the stability. It would have been obvious to prepare solutions of the instant claims, as previously outlined, without a sugar or sugar-based polyol, because Wolgemuth implies they are optional excipients. The motivation to exclude such a sugar would have been the desire to reduce the cost of a non-essential additive in the formulation.

Applicant argues all of the examples in Wolgemuth require mannitol, but acknowledges that the compositions may be interpreted to imply that the compositions therein do not require sugar or sugar-based polyol, but there fail to be any operable examples without such a component; there also fails to be any suggestion to substitute vinflunine for vincristine. These arguments are not persuasive. The exclusion of a sugar or sugar-based polyol would have been obvious because Wolgemuth implies the excipient is not required for stability of the formualtion. The suggestion to substitute would have been motivated by the recognition of the same art-recognized equivalent activities of the two closely related compounds (both are vinca alkaloids with anticancer activity), as pointed out in MPEP 2144.06 II.

6. Applicant's arguments with respect to the rejection of claims 8 and 14-15 under 35 USC 103 have been fully considered but they are not persuasive:

Claims 8 and 14-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over GlaxoSmithKline ("Prescribing Information: Navelbine (vinorelbine tartrate) Injection: 2002 Nov; pp. 1-17; IDS 1/22/2008 reference CA); Duflos et al. (US 6,127,377; 2000; IDS 10/4/2006 reference AB); and Wolgemuth (CA-2,001,643; 1990; IDS 10/4/2006 reference BC) as applied to claims 1-3, 7, 9 and 13; and 1-2, 4-7, 9 and 13 above, and further in view of Howell et al. ("Anti-vascular effects of vinflunine in the MAC 15A transplantable adenocarcinoma model"; 2001; British Journal of Cancer; 84(2): 209-295; IDS 10/4/2006 reference CG).

The rejection is maintained for the reasons of record.

Applicant argues Howell fails to disclose or suggest the aqueous vinflunine composition. This rejection is not based on Howell alone, but on the combination of references cited, as previously outlined.

Applicant further argues vinflunine has a lower solubility than vinorelbine, as a consequence it was not predictable that a stable aqueous solution of vinflunine having a concentration of between 25 and 30 mg/mL could be obtained since an aqueous solution at 70 mg/mL precipitates after 2 months of storage at 5 °C. It is not clear how the fact that a higher concentration precipitates renders a lower concentration as unpredictable, as argued. The position is maintained that it would have been obvious to optimize the composition based on the suggestions for the related teachings, leading to

an optimal concentration that would still be soluble; i.e., a relative increase in solubility would have been expected.

Conclusion

7. No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY P. THOMAS whose telephone number is (571)272-8994. The examiner can normally be reached on Monday-Thursday 6:30 a.m. - 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on (571) 272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Timothy P Thomas/
Examiner, Art Unit 1614

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614